

Introduction

In the field of neuroscience, diseases such as dementia have always been a focus. In MRI data, both normalized whole brain volume (nWBV) and estimated total intracranial volume (eTIV) hold significant importance in neurological research. This study aims to examine the dynamics of brain structure using two metrics: normalized whole brain volume (nWBV) and estimated total intracranial volume (eTIV). With these measures, the study will explore the effect of dementia on brain structure over time to support the development of interventions tailored to preserve cognitive function. The study will focus on the following research questions:

Research Question 1: How does normalized whole brain volume (nWBV) change over visits between dementia, converted, and nondemented groups?

Research Question 2: Does estimated total intracranial volume (eTIV) change over visits, and does this change differ between dementia, converted, and nondemented groups?

Data

The data used in the study are MRI results on patients with and without dementia across two visits. The dataset comprises a total of 294 rows and 16 columns. Based on the research questions, only the most relevant features will be utilized in further studies, as listed in Table 1 below:

Table 1. Description of Data

Variable	Descriptions
Subject ID	Subject identification
MRI ID	MRI exam identification
Group	Indicates whether the individual is diagnosed as Nondemented, Demented, or Converted. Categorical Variable.
Visit	The number of the visit at which the MRI was taken, either 1 or 2. Categorical Variable.
eTIV	Estimated Total Intracranial Volume. Numerical Variable.
nWBV	Normalized Whole Brain Volume. Numerical Variable.

	eTIV	nWBV
count	294.00	294.00
mean	1478.85	0.73
std	176.56	0.04
min	1106.00	0.65
25%	1347.25	0.70
50%	1461.50	0.73
75%	1569.00	0.76
max	2004.00	0.84

Table 2 - Summary of statistics

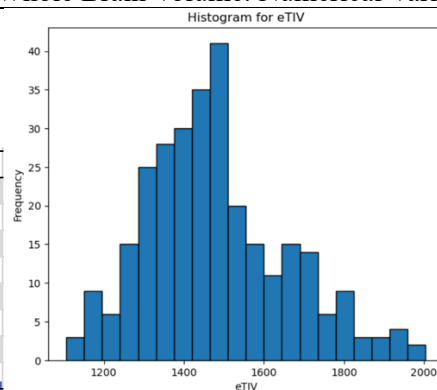


Figure 1

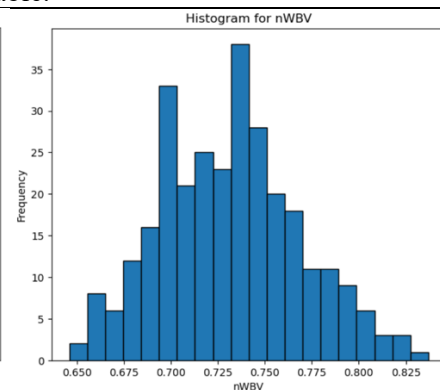


Figure 2

Table 2 presents the statistical summary of the numerical variables. Figure 1 and 2 displays the histograms for Estimated Total Intracranial Volume (eTIV) and Normalized Whole Brain Volume (nWBV), respectively. The eTIV histogram suggests a fairly normal distribution with a mean of

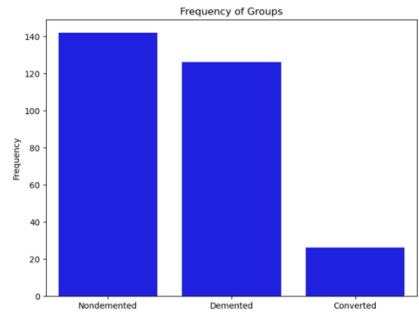


Figure 3

1478.85. The nWBV is important for understanding brain atrophy. It shows a central tendency across the population with a mean of 0.73. Both variables follow a normal distribution curve, indicating they can provide critical insights into dementia.

The categorical variables are “Group” and “Visit”. Figure 3 shows the frequency distribution across three categories: nondemented, demented, and converted. The majority of subjects are categorized as nondemented and demented, with a smaller proportion of subjects who have converted. In terms of

“Visit”, there are 150 individuals attending the first visit and 144 subjects at the second. This balance indicates a stable follow-up rate, which can ensure the reliability of this longitudinal analysis.

Mixed Effect for ANOVA 1

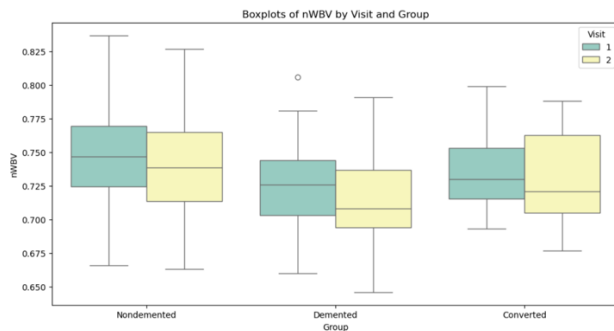


Figure 4

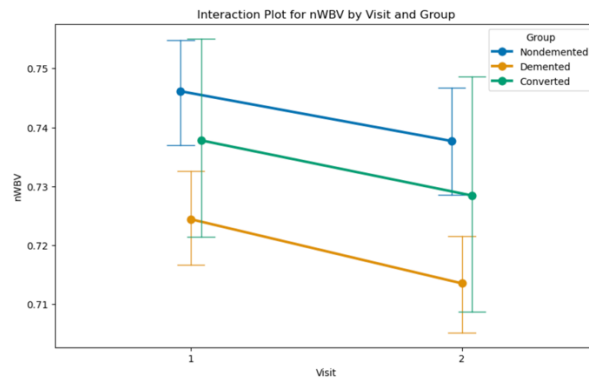


Figure 5

This section will focus on the first research question: How does normalized whole brain volume (nWBV) change over visits among demented, converted, and nondemented groups? The demented group showed a consistent mean decrease from 0.72 to 0.71 across two visits, both lower than the nondemented group. The boxplot in Figure 4 displays the nWBV distribution by visit and group. For the nondemented group, the median nWBV remains relatively stable across the two visits, while the demented group exhibits a decrease. Figure 5 is an interaction plot for nWBV by visit and group, which illustrates the changes in normalized whole brain volume across different groups over two visits. There is a notable decrease in nWBV from the first to the second visit. The relatively parallel lines may suggest there is no interaction effect; however, further tests are needed to confirm the presence of an interaction effect and changes. Therefore, a mixed-effect ANOVA is utilized with the dependent variable as “nWBV”, the within-subjects variable as “Visit”, and the between-subjects variable as “Group”.

Table 3 presents the mixed-effects ANOVA results with only the key numbers of the model. The mixed-effects ANOVA analysis investigated the influence of Visit and dementia status (Group) on nWBV. For the between-subjects factor, Group, the F-statistic of 6.712 and a p-value of 0.002 provide strong evidence to reject the null hypothesis that all “Groups” have the same mean nWBV. We can conclude that there is a statistically significant difference in nWBV across the different dementia status groups (nondemented, demented, converted). The within-subjects factor, Visit, has

a high F-value of 94.251 and a p-value < 0.001 , which is less than the significance level of 0.05. This provides strong evidence to reject the null hypothesis that nWBV does not change over time within individuals. The results indicate the changes in brain volume (nWBV) as time progresses. The η^2 value for Visit is 0.401, indicating a medium to large effect size.

Table 3. mixed effects ANOVA result

Source	F-statistics	P-value	η^2
Group(between-subjects factor)	6.712	0.002	0.087
Visit (within-subjects factor)	94.251	0	0.401
Interaction	1.534	0.219	0.021

In terms of interaction, the F-value of 1.534 and p-value of 0.219 indicate that the interaction effect between Group and Visit was not significant. This means that while groups differ and nWBV changes over time, the change is parallel across groups. This could be due to equipment error or another effect. The results of the study provide evidence that dementia status is linked to distinct brain volumes, which are changing over time. However, the change could be consistent regardless of dementia status, which requires further research with additional data.

Mixed Effect for ANOVA 2

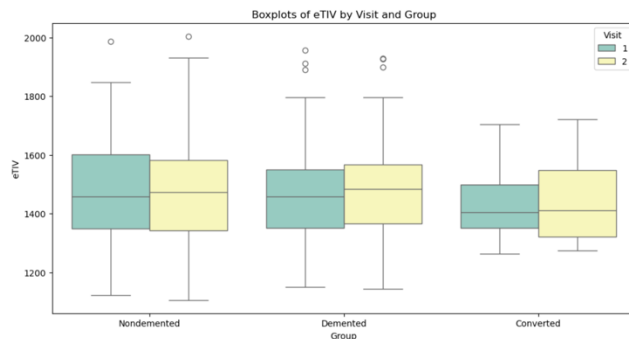


Figure 6

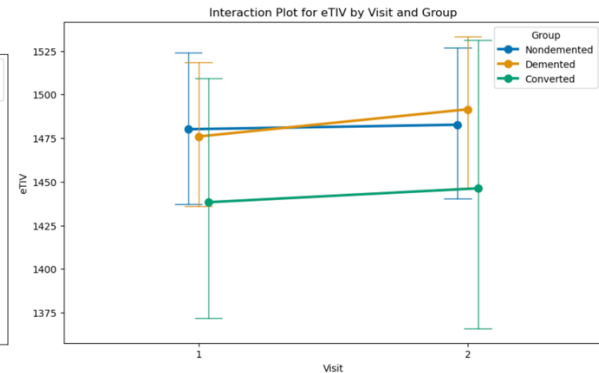


Figure 7

This section will focus on the second research question: Does estimated total intracranial volume (eTIV) change over visits, and does this change differ among demented, converted, and nondemented groups? Figures 6 and 7 are the boxplot and interaction plot for Estimated Total Intracranial Volume (eTIV) measurements across two visits for each group (nondemented, demented, and converted). The boxplot shows that the range and median do not exhibit significant change. The interaction plot indicates that eTIV is relatively stable across visits for all groups. There is an intersection between the nondemented and demented groups, which suggests the potential for interaction between group and visit. The figure hints at the potential stability of eTIV across groups, further statistical analysis is needed to confirm the results.

Table 4. mixed effects ANOVA result

Source	F-statistics	P-value	η^2
Group(between-subjects factor)	0.297	0.743	0.004
Visit (within-subjects factor)	9.225	0.003	0.061
Interaction	0.831	0.438	0.012

Table 4 is a brief summary of the mixed-effect ANOVA with the dependent variable as “eTIV”, the within-subjects variable as “Visit”, and the between-subjects variable as “Group”. The between-subjects factor “Group” has an F-statistic of 0.297 with a p-value of 0.743. The p-value is greater than 0.05, which means we do not have evidence to reject the null hypothesis that the

mean eTIV is equivalent across all groups. Regarding the within-subjects factor “Visit”, the F-statistic of 9.225 and the p-value of 0.003 provide strong evidence to believe that there is a statistically significant difference in eTIV across the two visits. This implies that the visit has a significant effect on eTIV within individuals. On the other hand, the interaction term between Group and Visit has an F-statistic of 0.831 and a p-value of 0.438. Since this p-value is greater than 0.05, we do not have evidence to reject the null hypothesis that there is no significant interaction effect between group and visit on eTIV. These results indicate that eTIV does not differ significantly among individuals with different dementia statuses. The results could be used in research and clinical practice, where eTIV is a control measure in studies of the brain.

Assumption Testing for both Mixed Effects ANOVA

1. Sphericity: The p-value is 1, which is greater than 0.05. Hence, assumption of sphericity is met.
2. Normality: Shapiro-Wilk test was conducted for both Visit, with p-values greater than 0.05. This shows that the data follow a normal distribution and the assumption of normality is met.
3. Homogeneity: Levene tests yield p-value greater than 0.05, indicating equal variances across groups and meeting the homogeneity assumption.

Therefore, all assumptions are met.

Statistical Power

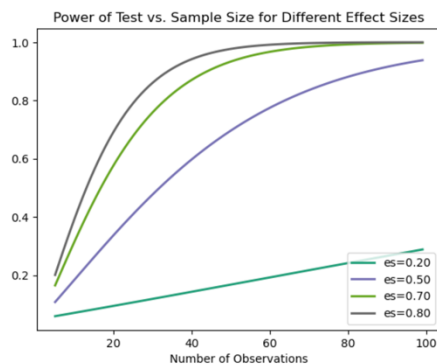


Figure 8

Figure 8 displays the power analysis plot to illustrate the relationship between sample size and power. To achieve a theoretical experiment with a power of 0.91, an alpha of 0.05, and an effect size of 0.7, we would need 46 observations.

Conclusions

The study focuses on the normalized whole brain volume (nWBV) and estimated total intracranial volume (eTIV) of individuals in different groups over two visits. We revealed significant changes within individuals across visits for nWBV but no significant differences in the rates of change among demented, converted, and nondemented groups. The study also revealed stability in eTIV, which remained consistent across groups and over time. The findings suggest that nWBV can be indicative of progression in dementia, as the rate remains consistent across different groups. The eTIV offers a stable measure that does not vary with the progression of time, which could be a reference point or control measure in future studies. The study can be helpful in the medical industry for aiding diagnosis and monitoring dementia. It also provides insights into different aspects of brain volumes. Further research can expand the study with a larger sample size and multiple visit times to assist in the diagnostics of dementia.